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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/072,159	02/05/2002	Bernard Bihain	29.US4.DIV	2627

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EXAMINER	
CHANDRA, GYAN	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 06/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/072,159	BIHAIN ET AL.	
	Examiner	Art Unit	
	Gyan Chandra	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 April 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *72,74,75 and 86-109* is/are pending in the application.

4a) Of the above claim(s) *86-89,94-97,99-105 and 107-109* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *72,74,75,90-93,98 and 106* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/1/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

5.02

DETAILED ACTION

Status of Application, Amendments, And/Or Claims

Claim 73, and 76-85 are canceled. The amendment of claim 72 and the addition of new claims 86-109 have been made of record.

Claims 86-89, 94-97, 99-105, and 107-109 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Invention.

Claims 72, 74-75, and 86-109 are pending and are examined on the merit to the extent that they read on the elected Invention ApM1 which is sequence ID NO: 11. Claims 72, 74, 75, 90-93, 98 and 106 read on the elected invention.

The amendment of specification indicating the priority to the U. S. Pat. No 6,344,441 has been entered.

The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Information Disclosure Statement

The information disclosure statement filed 4/1/2005 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, the crossed references therein have not been considered.

Response to Arguments

Claim Rejections - 35 USC § 112, second paragraph

Applicant's arguments, see Remarks, filed 4/1/2005, with respect to the previous office action mailed on 12/27/2004 have been fully considered and are persuasive. The claim rejections of 72, 74 and 75 under 35 USC § 112, second paragraph has been withdrawn due to the amendment of claims 72, and in consideration of the sequence alignment provided by Applicants in support of their arguments.

Claim Rejections - 35 USC § 112, first paragraph

Applicant's arguments filed on 4/1/2005, with regard to claims 72, 74 –75, and 90 (new claim) rejected under 35 USC § 112, first paragraph, have been fully considered but they are not persuasive. Applicants argue that the invention is enabled for partitioning of dietary lipids between the liver and peripheral tissues (Remarks, page 8) upon administering ApM1, and therefore, the invention is enabled for underlying causes for all "obesity-related" diseases. Applicants cite Diez and Iglesias (2003) and Kondo et al (2002) that ApM1 plays role in diabetes and obesity. Obesity is a highly complex polygenic disease and involves genetic and environmental factors. As Bays (2004) says that to date many agents have been tried in the area of CNS/ leptin/ gastrointestinal-neural/ endocrine pathways to reduce obesity in some subjects but not in all. Basy further says that a number of agents have been used to reduce or treat obesity in subjects, but due to complexity of the disease it would be impossible to predict at this point which agent or agents will eventually prove to revolutionize obesity treatment.

Therefore, it would be unpredictable to make and/ or use the invention commensurate in scope with these claims.

Upon further consideration, a new ground(s) of rejection is made in view of Applicants addition of claims 86-109.

New Ground of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claims 91 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method of increasing the partitioning of dietary lipids between the liver and peripheral tissues comprising the administration of an agent having at least 80% homology with the polypeptide of amino acid SEQ ID NO: 11 and a biologically active homolog of claimed sequences. The claims do not require that the polypeptide possess any particular conserved structure, or any other disclosed distinguished feature. Thus the claims are drawn to a genus of nucleic acids that is defined solely by sequence homology.

To provide undisclosed possession of a claimed genus, the specification must

provide sufficient distinguishing identifying characteristics for the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the chemical product, or any combination thereof. There is no discloser for identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

This is a written description rejection, rather than an enablement rejection under 35 U.S.C. 112, first paragraph. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Vas-Cath Inc. V. Mahurka, 19 USPQ2d 1111, states that applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, for purposes of the written description inquiry, is *whatever is now claimed* (see page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (see Vas-Cath at page 1116).

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a

substantial portion of the genus. *Regents of the* University of California v. Eli Lilly & Co., 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In *Regents of the* University of California v. Eli Lilly (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that, while applicants are not required to disclose every species encompassed by a genus, the description of the genus is achieved by the recitation of a representative number of species falling within the scope of the claimed genus. At section B(1), the court states an adequate written description of a DNA ... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention.

As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolating it. The compound itself is required. See Fiers v.Revel, 25USPQ2d 1601 at 1606 (CAFC 1993) and Amgen v.Baird, 30 Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 148 at 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provides only the bovine sequence. Therefore, only the isolated polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 11, but not the breadth of the claims meet the written description provision of 35 U.S.C.

§ 112, first paragraph.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Claim 91 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of increasing the partitioning of dietary lipids between the liver and peripheral tissue comprising the administration of ApM1, does not reasonably provide enablement for a method of increasing the partitioning of dietary lipids between the liver and peripheral tissue comprising the administration of a polypeptide of at least 80% sequence homology with the SEQ ID NO: 11. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and /or use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention; 2) state of the prior art; 3) relative skill of those in the art; 4) level of predictability in the art; 5) existence of working examples; 6) breadth of claims; 7) amount of direction or guidance by the inventor; and 8) quantity of experimentation needed to make and/or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art

to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Additionally, the courts have determined that "... where a statement is, on its face, contrary to generally accepted scientific principles", a rejection for failure to teach how to make and/or use is proper (In re Marzocchi, 169 USPQ 367 (CCPA 1971). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977) and have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986).

The instant disclosure fails to meet the enablement requirement for the following reasons:

The Nature of the Invention: The claimed invention is drawn to a method of increasing the partitioning of dietary lipids between the liver and peripheral tissues comprising the administration of an agent having at least 80% homology with the polypeptide of amino acid SEQ ID NO: 11 and a biologically active homolog of claimed sequences.

The state of the prior art and the predictability or lack thereof in the art:

ApM1 is a polypeptide secreted from adipocytes and plays a role in reducing plasma triglyceride. The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinants to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These regions can tolerate only relatively conservative substitutions or no substitution (see Bowie et al., 1990, Science 247: 1306-1310, page. 1306, column 2, paragraph2; Wells, 1990, Biochemistry 29:8509-8517). The specification does not disclose any working example that can predict functional out come of a mutation in ApM1 protein. Once a mutation has been made in a ApM1 protein, it will require large amount of experimentation to determine its functional consequences. There is no guidance to how well a mutant would impact reducing plasma triglyceride levels in vivo so that it can be used in a patient to increase partitioning of dietary lipids between the liver and peripheral tissues. It is unpredictable to substitute an amino acid with another amino acid without any loss in functionality.

The amount of direction and guidance present and the presence or absence of working examples: Given the teachings of unpredictability found in the art, detailed teachings are required to be present in the disclosure in order to enable the skilled

artisan to practice the invention commensurate in scope with the claims. These teachings are absent. Applicants generated a table (page 17) with percent homology with other known proteins such as acrp-30, Adipo Q, or cerebellin. Applicant's working hypothesis is that making mutants in ApM1 would lead in identifying agents for treating various pathological conditions related to diabetes and obesity. it will require to a large number of experimentation to make innumerable mutations in ApM1 and to see any functional effect, in any patient.

The breadth of the claims and the quantity of experimentation needed: Because the claims encompass a method of increasing the partitioning of dietary lipids between the liver and peripheral tissues comprising the administration of an agent having at least 80% homology with the polypeptide of amino acid SEQ ID NO: 11 and a biologically active homolog of claimed sequences, in the light of the teachings of the unpredictability found in the art discussed and because of the supra lack of sufficient teachings in applicants disclosure to overcome those teachings, it would require undue experimentation by one of skill in the art to be able to practice the claimed invention.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gyan Chandra whose telephone number is (571) 272-2922. The examiner can normally be reached on 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on (571) 272-0829. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gyan Chandra
AU 1646
05 June 2005

JANET ANDRES
PRIMARY EXAMINER